## REMARKS

Applicants thank the Examiner for the thorough consideration given the present application.

Claims 32, 34-43 and 47-84 are pending. Claims 32, 69 and 74 are independent.

Claims 32, 34-40, 43, 47-60, 63 and 69 are amended. Claims 33 and 44-46 are canceled. Claims 74-84 are new. Reconsideration of the application, as amended is respectfully requested.

### Rejection Under 35 U.S.C. § 112, $2^{nd}$ Paragraph

Claims 36, 46 and 59 stand rejected under 35 U.S.C. § 112, $2^{nd}$ Paragraph. This rejection is respectfully traversed.

The Examiner has set forth certain instances wherein the claim language is not clearly understood.

In order to overcome this rejection, Applicants have canceled claim 46 and amended claims 46 and 59 to correct each of the deficiencies specifically pointed out by the Examiner. Applicants respectfully submit that the claims, as amended, particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

### Basis for the Amendments

Regarding amended claim 32, the basis for the modifications compared to previous claims 32 and 33 is as follows. The claim now requires the at least one conductive member to be "disposed in said microchannel or *forming at least a part of a wall of said microchannel*". Basis for this alternative feature is provided for example by the embodiment of Figure 13, as described at page 13 lines 4-5.

Claim 32 requires that the conductive member has "a specific geometrical shape so as to provide in the microchannel a surface of the member wherein the normal to the surface has a component parallel to and a component perpendicular to the direction of the electric field in said microchannel". Basis for this amendment is to be found on page 6 lines 13-16, for example.

Claim 32 requires that the conductive member comprises a perm selective ion conducting material. Basis for this amendment is to be found in original claim 10 which stated that the conducting means may consist of an ionic conducting material, and more specifically at page 18 lines 15-16 which refers to a perm selective ion conducting material, with a perm selective cation conducting material being indicated as an optional feature. There is further basis at page 14 lines 11–12 and page 20 lines 21–22.

Claim 32 no longer refers to an "electrically" conductive member, which was the term used in previous claim 33. It therefore reverts more closely to original claim 1 which referred to "conducting means".

Basis for the amended version of claim 69 is essentially the same as that explained above in relation to claim 32.

Claim 74 is a new independent claim which we are including in case the Examiner is not prepared to accept claims 32 and 69, but is prepared to accept the more specific definition of claim 74.

Claim 74, like claim 32, includes the alternative feature of the conductive member forming at least part of a wall of the microchannel. As with claim 32, basis is provided by Figure 13 and its description at least. The claim also requires that the conductive member comprises a perm selective ion conducting material, and again basis is the same as that mentioned above in relation to claim 32.

Claim 74 states that the conductive member has a characteristic dimension which is its dimension measured parallel to the electric field. Basis for this definition is to be found on page 10 lines 8-9.

Claim 74 then requires that this characteristic dimension is at least 10 micrometres. Basis for a lower limit of 10 micrometres is provided at least at page 14 lines 27-28, where it is stated that the characteristic dimension should be for most applications between 10 and 500 micrometres. We have not used the upper limit of 500 micrometres in the claim, and I believe this is justified at least by the example given at page 9 line 14 of a particle size of 1000 micrometres, i.e. 1 mm.

Claim 74 specifies that "a flow passage is defined between said surface of the conductive member and another conductive member or between said surface and a portion of the wall of the said microchannel". The creation of a flow passage in this way in the system is a feature of all the embodiments. The flow passage is self-evidently that part of the microchannel which is available for flow.

Claim 74 refers to the flow passage as having a "minimum" diameter. In most of the embodiments the diameter of the flow passage, i.e. the width of the microchannel available for flow, varies along the length of the passage. See for example Figures 2, 3, 4, 5, 8, 9, 10, 11, 14, 15, 17, 18, 19 and 20. In the embodiment of Figure 2, for example, spherical conducting members 18 are provided in a channel of rectangular cross-section (see page 11 lines 9-15). Thus the width of the flow passages defined between adjacent spheres and between a sphere and the wall, i.e. the width of a respective flow passage, varies in the direction of flow. It is stated at page 11 lines 11-12 that the "distance between particles and between particles and the wall is approximately equal to $a_{char}$". At page 10 line 14 it is indicated that $a_{char}$ is "0.5 times $d_{char}$" where $d_{char}$ is the characteristic dimension of the element, i.e. its dimension measured parallel to the direction of the electric field (page 10 lines 8-9). Looking at Figure 2, it will be seen that the minimum diameter of the flow passage is about half the dimension of the spheres and so it is clear that the reference at page lines 11-12 to the "distance between particles and between particles and the wall" is a reference to the minimum distance, i.e. the minimum diameter of the flow passage.

Finally, claim 74 requires that the flow passage has a minimum diameter of "at least 1/16 of the characteristic dimension of the conductive member". Various examples of this minimum diameter, or space, are given in the description of the embodiments from page 11 line 9 to page 14 line 5. In the passage at page 14 line 30 to page 15 line 1 it is stated that for "applications where predominantly directed EO2 pumping is desired, the space between the conducting particles 18, and between the conducting particles 18 and the channel walls 20a, should be between 1/8 and ½ $a_{char}$". At page 15 lines 7-8 it is indicated that if "mixing should also be obtained, the distances could be up to 2 $a_{char}$". Thus a minimum space, or flow passage diameter, of 1/8 $a_{char}$ is specified. Of course, since $a_{char}$ is one half of $d_{char}$ (page 10 line 14), this means that

the minimum diameter of the flow passage is 1/16 of $d_{char}$, i.e. 1/16 of the characteristic dimension of the conductive member, as specified in claim 74.

Basis for new claim 75 is at page 14 lines 26-27.

Basis for new claim 76 is at page 15 lines 6-7.

Basis for new claim 77 is at page 10 lines 5-6.

Basis for new claim 78 is at page 14 lines 21-23.

Basis for new claim 79 is at page 14 lines 23-24.

Basis for new claim 80 is at page 10 line 29.

Basis for new claim 81 is at page 16 lines 8-9.

Basis for new claim 82, particularly for the feature that the microchannel has an inlet and outlet, is provided at page 11 lines 3-5. Flow adjacent to the surface of the conductive member along the microchannel is a feature of many of the embodiments.

Claim 83 is a method claim directed to the operation of the system of claim 74. It therefore finds the basis in the same way as claim 74 itself.

Basis for claim 84 is provided by equation 3 on page 20 line 6.

**Claim Rejections under 35 U.S.C. § 102(b) and § 103**

Claims 32, 33 and 69-73 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Squires et al. ("Microfluidic Pumps and Mixers Driven by Induced-Charge Electro-osmosis, 2001"; hereinafter "Squires"). This rejection is respectfully traversed. Claims 32, 69 and 73 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Theeuwes. These rejections are respectfully traversed.

Claims 34-65 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Squires et al. in view of Dukhin and Bazant and claim 68 stands rejected as being obvious over Squires in vew of Dukhin and Goodson et al. Claim 66 stands rejected as being obvious over Theeuwes in view of Mischuk and Goodson et al. Although claims 64-67 are discussed in the rejection of claim 34-65 based on Squires et al. in view of Dukhin and Bazant, the context is not clear.

On page 4 of the Office Action, the Examiner objected to the broadest claims as being anticipated by Squires' paper "Microfluidic Pumps and Mixers Driven by Induced-Charge

Electro-osmosis". Whilst our clients maintain their position that secondary electroosmosis is not disclosed by Squires, in order to advance prosecution the enclosed independent claims 32, 69 and 74 contain additional limitations which further distinguish the invention from Squires. In particular, each of these claims requires that the conductive member comprises a perm selective ion conducting material.

Squires, on the other hand, uses metallic conductors. As noted on page 24 of the Office Action, at paragraph 11 a), the Examiner has correctly noted that in "Squires the electrically conducting materials are metal objects, such as wires or metal strips, or metallic or metallic and dielectric coatings on metal objects". See for example the section "B. Mixers" on page 7 of Squires, where Figure 9 is described as having conducting posts in the form of "fixed metallic wires", and Figure 10 is described as showing "metal stripes embedded in the channel walls in between the electrodes". Furthermore, Figure 6b shows a cylinder with a metallic coating. Figure 14 on page 9 shows a "patterned metallic surface", further described at the bottom of the first column on page 9 as "a grooved metallic slab". In the summary in the second column on page 9 it is stated that the "simplest designs are essentially judicious arrangements of metal wires in microfluidic channels". In view of all these references to the use of metal conductors, it is clear that the other examples which are described as having "conductive" spheres or cylinders are also references to metallic conductors.

Claims 32, 69 and 74 are therefore clearly novel over Squires, because they require the conductive member to comprise a perm selective ion conducting material.

Regarding the question of obviousness, it is to be noted that Squires addresses the problem of how to obtain a pumping effect using metallic conductors. In the section headed "E. Asymmetric Conductors" at the bottom of page 5 he states that by "breaking the fore-aft symmetry of a conductor in a DC or AC applied field in a variety of ways, a net osmotic flow along the field axis (for a fixed object) or net phoretic swimming velocity (for a free object) can be easily produced, as illustrated in Figure 6". This breaking of the symmetry is "accomplished by coating one side of the conductor with dielectric or a different metal, or by simply changing the shape to break fore-aft symmetry". Examples are shown and described in Figure 6 on page 6.

The present invention can also create an "asymmetric" pumping effect but in this case the effect is achieved by using a perm selective ion conducting material. The use of such a material to achieve a pumping effect (whether for flow from an inlet to an outlet or for mixing) is not disclosed by Squires and clearly the Squires paper envisages only metallic conductors and ways of achieving pumping effects using these metallic conductors. The use of a perm selective ion conducting material achieves the desired flow under the action of secondary electroosmosis, as specified in each of claims 32, 69 and 74. The use of such a material to harness the secondary electroosmosis phenomenon to achieve pumping is not disclosed nor remotely suggested by Squires.

Further concerning the non-obviousness of claim 74 in particular, it is correctly noted by the Examiner in the paragraph bridging pages 13 and 14 of the Office Action, that Squires uses a conducting cylinder having a radius of 1 micrometer, i.e. a diameter of 2 micrometers. Claim 74 of the present application on the other hand specifies a minimum dimension (which would be the diameter in the case of a cylinder) of 10 micrometers. This is five times greater than the diameter disclosed by Squires, and there is no suggestion in Squires of the use of a cylinder of this much greater diameter. This distinction is of course in addition to the use of a perm selective ion conducting material rather than a metal. Taken together, the use of this material and this minimum size to exploit the secondary electroosmosis phenomenon to achieve pumping, are clearly far beyond mere optimisation and so support a non-obviousness finding in relation to claim 74.

On page 8 of the Office Action the Examiner has objected to previous claims 32, 69 and 73 as being anticipated by US 4540403 (Theeuwes) as evidenced by two papers by Mischuk. He has stated that Theeuwes discloses a microfluidic system comprising a microchannel and a pump arranged to electroosmotically cause flow, but Theeuwes does not mention whether the fluid flow is at least in part due to secondary electroosmosis. The Examiner has suggested that "this appears to be an intended use of which the pump in Theeuwes is capable" and has also stated that "in light of Mischuk the pumping in Theeuwes is inherently secondary electroosmosis as the pump in Theeuwes may comprise an ion exchange material". The Examiner has pointed out that Theeuwes discloses an ion exchange material at column 3 lines 51-63.

Theeuwes relates to a parenteral delivery system in which charge bearing agents are delivered across an inner wall 54 in order to introduce a beneficial agent, i.e. a drug, to a passageway 56. Theeuwes suggests two distinct types of material which may be used to form the inner wall 54. These are: (a) an ion exchange material, or (b) a porous material (column 3 lines 55-57). Regarding (a), it is stated that the apparatus operates to "deliver drug by electrodialysis when internal wall 54 is formed of an ion exchange material" (column 4 lines 34-36). Regarding (b), in relation to the use of a porous material, it is stated that "electro-transport apparatus 30 operates to deliver drug 53, when wall 54 is formed of a porous material ... in an electric field by electroosmosis" (column 4 lines 48-52). Examples of suitable porous materials are quartz, glass or ceramic (column 5 lines 16-18).

Thus, Theeuwes discloses delivery by (a) electrodialysis and (b) electroosmosis. The relevance of each of these processes as taught by Theeuwes to the present invention will be discussed below.

First, in relation to Theeuwes' (b) electroosmostic process, this is disclosed as involving the use of a porous material and the examples given are quartz, glass or ceramic. There is no suggestion that the porous material could be an ion exchange material. Amended claims 32, 69 and 74 are therefore clearly distinguished over version (b) of Theeuwes involving electroosmosis. In addition, there is no disclosure in Theeuwes that any part of the porous material would have the requirement in each of these claims of providing "a surface of the member wherein the normal to the surface has a component parallel to and a component perpendicular to the direction of the electric field". The electroosmosis referred in Theeuwes is conventional electroosmosis and not secondary electroosmosis as required by the claim.

Turning then to Theeuwes' (a) electrodialysis process, this involves the use of an ion exchange material, which is another term for a perm selective ion conducting material as required by amended/new claims 32, 69 and 74. However, the material is formed as a flat membrane and so there is no member with a surface "wherein the normal to the surface has a component parallel to and a component perpendicular to the direction of the electric field in said microchannel, such as to cause fluid in said microchannel to flow under the action of secondary electroosmosis" (claim 32), as required by each of claims 32, 69 and 74. Indeed, Theeuwes

makes no suggestion that in this version of his invention there is any electroosmosis, rather he refers to electrodialysis.

It will be appreciated from the present application that it is a necessary feature of secondary electroosmosis for a space charge region (SCR) to be generated (see page 18 lines 4-26 and Figure 21 and its description on page 8 lines 28-31). It is to be noted that Figure 21 shows an embodiment of a member with a surface wherein the normal to the surface has a component parallel to and a component perpendicular to the direction of the electric field. When such a member is provided in a microchannel then secondary electroosmotic flow in the microchannel occurs. However, in the case of a flat membrane, such as that of Theeuwes' ion exchange material embodiments, the space charge region will be generated at the surface only. Since the surface of the membrane is not disposed in a microchannel nor does it form at least part of a wall of a microchannel, even if there are surface flow effects, there is no secondary electroosmotic flow *in a microchannel*, as required by claims 32, 69 and 74. At the top of page 9 of the Office Action, it is stated "the Examiner broadly construes microchannel to a channel having a dimension on the order of microns". As seen in Figures 3, 4 and 5 of Theeuwes the internal space 51 on one side of the membrane and the passageway 56 on the other side of the membrane are large volume areas and cannot in any interpretation be regarded as microchannels.

At paragraph 5 on page 8 of the Office Action, the Examiner objected to claims 32, 69 and 73 as being anticipated by Theeuwes as evidenced by Mischuk 's paper "Electro-osmosis of the second kind near heterogeneous ion-exchange membrane". Mischuk discloses that "electro-osmosis of the second kind also appears near a flat heterogeneous interface (for example near an ion-exchange membrane)" (page 76, first complete paragraph of second column). The effect of the electroosmosis is to create electroosmotic whirlwinds near the surface (page 76 column 2 lines 23 – 24, page 78 column 2 lines 13 – 16). Therefore, even if a similar effect occurred using the ion exchange membrane proposed by Theeuwes, this would be an effect at the surface, and not in a microchannel as required by amended/new claims 32, 69 and 74. There would be no flow caused in a microchannel as required by these claims. Moreover, the membrane discussed by Mischuk is heterogeneous (see Figure 2 on page 79) in order to obtain the electroosmotic whirlwinds, unlike the conventional ion exchange membrane of Theewues.

The ion exchange membranes of Theeuwes may however include pores with a diameter in the nanometer range. Typical pore sizes of ion exchange membranes are of the order of 10-20 nanometers. There can be no secondary electroosmosis in pores of this size. There are at least two reasons.

First, it is a condition for secondary electroosmosis for there to be an interface between free liquid and solid. In pores of the very small diameter discussed there will be a so-called electric double layer generated on the internal surfaces of the pores. Because the pores have such a narrow diameter, the electric double layer will overlap and so the required interface between a free liquid and the solid necessary for secondary electroosmosis is absent.

The second reason why there will be no secondary electroosmosis in the nanopores of the membrane arises from the fact that the membrane has a much higher conductivity than the surrounding liquid. This effectively means that any electric field in the nanopores is "short-circuited". This removes a necessary condition for concentration polarisation (and hence for charge build up). Therefore, in a membrane with nanopore sized channels, charge will be induced at the surface, but not to any significant degree on features inwardly of the surface inside the pores. Therefore, even if the nanopores of Theeuwes' membrane are regarded as the microchannels of the claims of the present application, there will be no secondary electroosmotic flow in these pores.

It is clear from the above that each of claims 32, 69 and 74 is patentably distinguished from Theeuwes, because Theeuwes does not disclose a conductive member comprising a perm selective ion conducting material and having a surface wherein the normal to the surface has a component parallel to and a component perpendicular to the direction of the electric field in the microchannel, such as to cause fluid in the microchannel to flow under the action of secondary electroosmosis.

Claims 32 and 69 include the additional feature that the conductive member has "a specific geometrical shape" so as to provide this surface in the microchannel. This structural feature provides a further distinction over the ion exchange membrane of Theeuwes, in which the nanopores will be generally tortuous and disorganised in their orientation, and this is to some extent illustrated in Figures 3, 4 and 5 of Theeuwes (although with a somewhat misleading

distortion of the scale). Tortuous and randomly arranged pores do not have a specific geometrical shape which provides the surface required by the claims.

Claim 74 includes a further structural feature, in that it defines the minimum diameter of the flow passage as being at least 1/16 of 10 micrometres, i.e. at least 625 nanometers. Ion exchange membranes are made of materials where the pores are generally just a few nanometers, and certainly at least an order of magnitude less than 625 nanometers. Thus, claim 74 is further distinguished from the Theeuwes system.

At the top of page 21 of the Office Action, the Examiner has suggested that it would have been obvious to use a pump as taught by Squires in the invention of Theeuwes. If this were possible, it would mean *replacing* the membrane of Theeuwes by the metal conductors of Squires, resulting in a system not using perm selective ion conducting material as required by amended/new claims 32, 69 and 74. Thus even if this was an obvious modification to make to Theeuwes, it would not result in the present invention.

Applicant respectfully submits that the claims define the invention over both Squires and Theeuwes for the reasons set forth above. Moreover, no other prior art of record cures the deficiencies of Squires and Theeuwes noted above. Accordingly, reconsideration and withdrawal of these rejections are respectfully requested.

**Conclusion**

In view of the above amendments, it is believed that the pending application in condition for allowance. Applicants respectfully request that the pending application be allowed.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Chris McDonald, Registration No. 41,533 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§ 1.16 or 1.147; particularly, extension of time fees.

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Respectfully submitted,

By PCL

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